PATENT
Attorney Docket No. 012712-256

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of)
)
Darrell R. ANDERSON et al)
)
Serial No. 08/746,361)
)
Filed: November 8, 1996)
)
For: IDENTIFICATION OF UNIQUE)
BINDING INTERACTIONS BETWEEN)
CERTAIN ANTIBODIES AND THE)
HUMAN B7.1 AND B7.2)
CO-STIMULATORY ANTIGENS)

Group Art Unit: 1644

Examiner: P. Gambel

§132 DECLARATION BY DARRELL R. ANDERSON, Ph.D.

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

I, Darrell R. Anderson, Ph.D., declare and state as follows:

(1) That I am an inventor of the above-identified patent application.

(2) That I am aware that the Examiner has concluded that there is insufficient information of record to distinguish the claimed monoclonal antibodies that specifically bind human B7.1 antigen, which do not inhibit the binding of human B7.1 antibody to CTLA-4 antigen, from the monoclonal antibody disclosed by de Boer, U.S. Patent 5,747,034.

(3) That I believe the experiments discussed below provide convincing evidence that the monoclonal antibody of de Boer possesses a different binding specificity than the anti-B7.1 monoclonal antibodies of the present invention.

(4) Specifically, I compared the ability of the de Boer antibody (B7-24) to a monoclonal antibody of the invention (p16C10), and another anti-B7.1 antibody, L307.4. These antibodies were compared for their ability to inhibit the binding of B7Ig to CTLA4Ig. In this experiment, an ELISA plate was coated with CTLA4Ig, and serially diluted B7-24, p16C10, or L307.4 were then mixed with B7Ig-Bio. It can be seen from the results in Figure 1 that both the prior art antibodies, i.e,. B7-24 and L307.4, substantially inhibited the binding of B7Ig to CTLA4Ig. By contrast, p16C10 had no effect on the binding of B7Ig to CTLA4Ig. Therefore, it can be seen that the de Boer antibody (B7-24), as well as the other prior art antibody, unlike the claimed anti-human B7.1 antibodies, inhibited the interaction of B7.1 with CTLA-4.

(5) Also, another ELISA experiment was conducted wherein the binding of B7-24 and p16C10 on B7 binding were compared. In this experiment, a B7Ig coated plate was contacted with serially diluted B7-24 and p16C10, and were mixed with p16C10-Bio. The results of this ELISA are in Figure 1. These results show that B7-24 had no effect on the binding of p16C10 to B7 antigen, and which indicates that these antibodies bind distinct anti-B7.1 epitopes.

(6) Further, Experiment 3 compares the direct binding of B7-24 and p16C10 to B7.1 antigen based on absorbence at different μg/ml concentrations. It can be seen further from these results that the antibody of de Boer (B7-24), and the invention (p16C10) exhibit distinct binding characteristics.

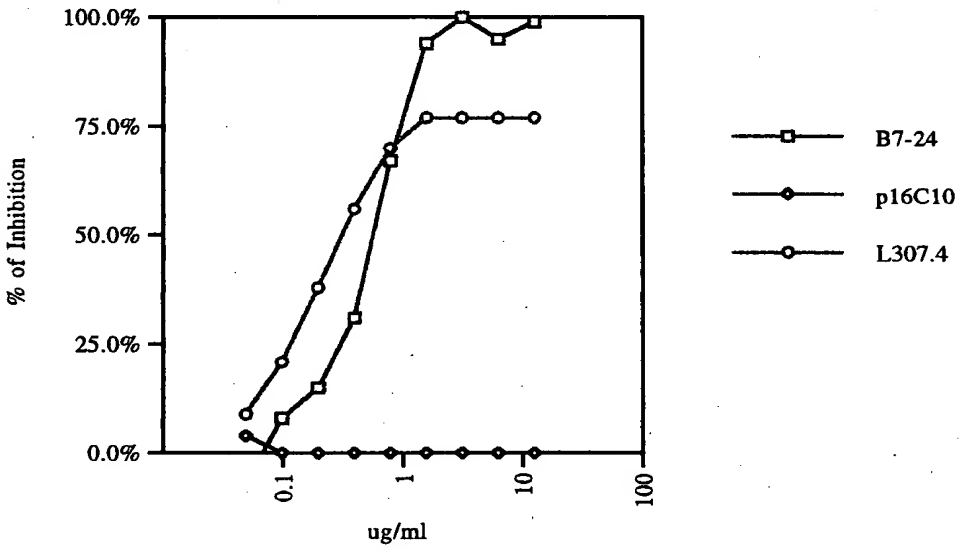
(7) In conclusion, I am of the opinion that Experiments 1 and 2 provide convincing evidence that the anti-human B7.1 monoclonal antibodies of the present invention exhibit distinct binding specificity than those of de Boer.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

_____ _____

Date Darrell R. Anderson

Inhibition on B7Ig Binding to CTLA4Ig

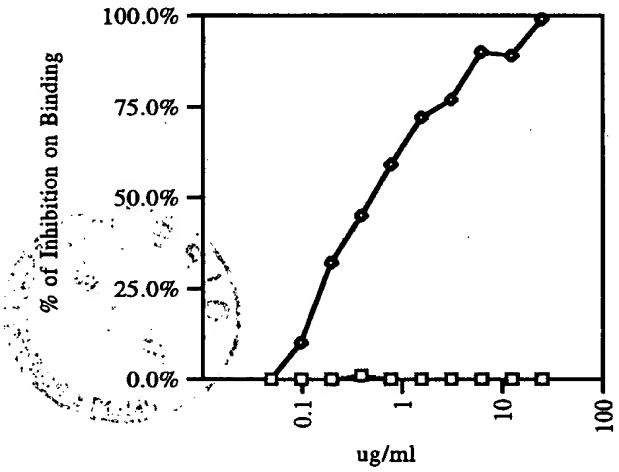


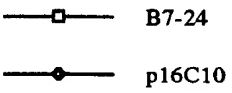
The ELISA Plate was coated with CTLA4Ig, the serially diluted B7-24, p16C10, and L307.4 were mixed with B7Ig-Bio,

FIGURE 1

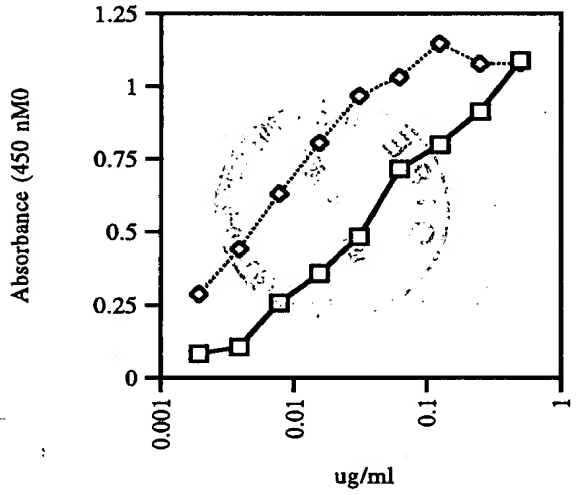
FIGURE 2

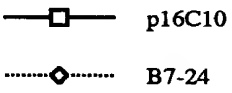
Comparison of B7-24 and p16C10 on B7 Binding





On B7Ig coated plate, serially diluted B7-24 and p16C10 were mixed with p16C10-Bio.





Direct Binding

FIGURE 3